

REMARKS

Upon entry of the present amendments, claims 1-18 and 20-38 will be pending. The Office has examined claims 1-18 and 20-28. Claims 1, 16, 17 and 24 have been amended. New claims 29-38 have been added. Claim 19 has been canceled without prejudice or disclaimer.

Applicants have amended claims 1, 16, 17 and 24 to more particularly point out the claimed subject matter. Support for the amendments can be found in the specification, for example, at page 36, line 23-30, and page 37, lines 16-22.

Applicants have added new claims 29-38. Support for the new claims can be found in the specification, for example, at page 9, lines 20-26; page 10, lines 16-24; page 11, lines 4-10; page 11, lines 14-19; page 11, lines 21-24; page 11, line 29 to page 12, line 5; page 12, lines 19-30; page 13, lines 10-17; page 13, lines 22-30; and page 6, lines 19-29.

The abstract has been replaced with a new abstract.

No new matter has been added.

Allowable subject matter

Applicants note that no rejections have been made to claims 16 and 17 in this Office Action. Therefore, Applicants submit that these claims are allowable.

Further, if the Office raises any rejections against claims 16 and 17 in a subsequent Office Action, Applicants submit that the next Office Action cannot be made final, as Applicants have not had an opportunity to address any rejections to these claims in reply to the present Office Action.

Objection to the abstract under 37 C.F.R. § 1.72

On page 2 of the Office Action, the Office objects to the abstract amended in the reply to the previous Office Action, dated November 29, 2006, and suggests: "Applicants should amend the abstract so that it corresponds to at least one independent claim. For example, Applicants should describe/surmise the series of method steps *a* through *g*. *See* 37 C.F.R. § 1.72."

Applicant respectfully note that 37 C.F.R. § 1.72 does not require the abstract to correspond to at least one independent claim or to describe every step recited in the claim. 37 C.F.R. § 1.72(b) only states that “[t]he purpose of the abstract is to enable the United States Patent and Trademark Office and the public generally to determine quickly from a cursory inspection the nature and gist of the technical disclosure.”

For the purpose of moving this application forward, Applicants have presented a new abstract to replace the previous one, as suggested by the Examiner. Applicants submit that the new abstract fully complies with the requirements of 37 C.F.R. § 1.72.

Claim rejection under 35 U.S.C. § 102(b)

At pages 2-4 of the Office Action, the Office rejects claims 1-15, 20-24 and 26-28 as allegedly being anticipated by Sawyer et al., J. Immunological Methods 204:193-203 (1997) (“Sawyer”). Applicants disagree, and respectfully traverse this rejection.

Claims 1-15. Claims 1-15 are directed to methods of selecting phage that encode a target binding protein from a plurality of display phage. The methods include forming a mixture that contains a plurality of diverse display phage, a target, and a support, and forming phage immobilized to the support, each of which comprises a phage which binds the target and the target immobilized to the support. Phage that do not bind to the target are separated from phage immobilized to the support via binding to the target. The methods include contacting host cells with the phage immobilized to the support so that the host cells are infected by the phage immobilized to the support to yield a first population of infected cells (e.g., step (d) of claim 1). Replicate phage are produced in the presence of the target immobilized to the support, thereby forming replicate phage immobilized to the support via binding to the target (e.g., step (e) of claim 1). Replicate phage that do not bind to the target are separated from the replicate phage immobilized to the support. Host cells are contacted with the replicate phage immobilized to the support as part of the next step (e.g., step (g) of claim 1).

Applicants submit that Sawyer fails to disclose every element recited in the claims. For example, as pointed out by the Office, Sawyer discloses selecting antibodies to p185^{erb-2} from a

library of bacteriophage that display human Fabs (at page 193, Abstract). The selection is carried out by incubating the bacteriophage library with cell extract containing p185^{rb-2}. Phage displaying Fabs that bind to p185^{rb-2} are isolated by adding Dynabeads coated with a rat monoclonal antibody to p185^{rb-2}, such that phage bound to p185^{rb-2} bind to the Dynabeads (see page 195, right column and Figure 1). Sawyer describes the next steps:

Phage bound to the Dynabeads were separated ... Phage were eluted from the Dynabeads by incubation with 1 ml of 100 mM triethylamine ... The eluate (0.8 ml) was used to infect a 10-ml culture of log phase *E. coli* TGI cells which were then allowed to stand for 30 min at 37°C before plating onto a Nunc 243 X 243 mm dish of TYE agar (15 g bacto-agar, 8 g NaCl, 10 g tryptone, 5 g yeast extract per litre water) containing tetracycline (12 mg/ml). After overnight incubation at 37°C, the cells were scraped off into 200 ml 2 X TY broth ... The cells were pelleted by centrifugation ... Phage were precipitated from the culture supernatant ... The final pellet was resuspended in 2 ml PBS and 1 ml of this was used for the second round of selection. Four rounds of selection were performed (at page 195, right column, first and second paragraphs, emphases added).

First, Sawyer fails to teach contacting host cells with phage immobilized to a support via binding to a target immobilized to the support so that the cells are infected with the phage immobilized to the support, as required by the claimed methods (e.g., step (d) of claim 1). Sawyer teaches eluting phage from the Dynabeads prior to using the phage to infect host cells. That is, the host cells are contacted with phage that are no longer bound to the immobilized target (e.g., Dynabeads).

Second, since Sawyer only teaches eluting phage from the Dynabeads before infecting host cells with the eluted phage, Sawyer also fails to disclose contacting host cells with the replicate phage immobilized to the support so that host cells are infected with the replicate phage immobilized to the support, as recited in the claims (e.g., step (g) of claim 1).

Third, Sawyer fails to disclose producing replicate phage in the presence of the target immobilized to the support (e.g., step (e) of claim 1). To allow the infected host cells to produce replicate phage, Sawyer merely plates the infected host cells onto TYE agar plates. The list of agar ingredients does not include a target immobilized to a support.

Accordingly, Sawyer fails to disclose every element recited in claims 1-15, and does not anticipate these claims.

Claims 20-23. Claims 20-23 are directed to methods of identifying members of a bacteriophage library that have a desired binding property. The methods include providing a bacteriophage library that comprises a plurality of bacteriophage members, selecting a subset of the bacteriophage members (e.g., step (b) of claim 20), and infecting host cells with the members of the subset. The method includes amplifying members of the subset (e.g., producing replicate phage by host cells infected with members of the subset) under at least one of the following conditions: (1) fewer than 5000 progeny phage are produced for each phage member selected in step (b), (2) less than 4 hours elapses, and (3) the host cells divide less than 6 times (e.g., step (d) of claim 20). The methods also include selecting a subset of the amplified members, thereby identifying the desired members of the bacteriophage library.

Applicants submit that the Office fails to establish that Sawyer teaches every element of the claims. For example, Sawyer does not disclose that less than 5000 progeny phage are produced (e.g., step (d)(1) of claim 20), that the amplifying step occurs in less than 4 hours (e.g., step (d)(2) of claim 20), or that the host cells divide less than 6 times (e.g., step (d)(3) of claim 20). Thus, Sawyer does not anticipate claims 20-23.

Claims 24 and 26-28. Claims 24 and 26-28 are directed to methods of selecting a nucleic acid that encodes a binding protein from a library of display phage. The methods recite, *inter alia*, a step of contacting phage from the phage immobilized to the support with host cells so that the host cells are infected by the phage from the phage immobilized to the support (e.g., step (c)(iii) of claim 24).

As discussed above, Sawyer fails to teach contacting phage immobilized to the support with host cells. Therefore, Sawyer does not anticipate claims 24 and 26-28.

For at least the reasons stated above, Applicants submit that Sawyer does not anticipate claims 1-15, 20-24 and 26-28, and respectfully request withdrawal of this rejection.

Claim rejections under 35 U.S.C. § 103(a)

Rejection of claims 1-7, 9-15 and 20-28. At page 5 of the Office Action, the Office rejects claims 1-7, 9-15 and 20-28 as allegedly being obvious in light of Sawyer in view of U.S. Pat. No. 6,797,480 B1 ("Srivastava"). Applicants disagree and respectfully traverse this rejection.

As set forth above, Sawyer, the primary reference, fails to teach every element of the claimed methods. Moreover, nothing in Sawyer even remotely suggests a method that includes a step of contacting host cells with phage immobilized to a support so that the host cells are infected by the phage immobilized to the support (e.g., step (d) of claim 1); a step of producing replicate phage from infected cells in the presence of a target immobilized to a support (e.g., step (e) of claim 1); a step of contacting phage immobilized to a support with host cells so that the host cells are infected by the phage immobilized to the support (e.g., step (c)(iii) of claim 24); or a step of producing phage from infected cells in the presence of a target (e.g., step (c)(iv) of claim 24). Nor does Sawyer suggest a method carried out in a manner such that less than 5000 progeny phage are produced (e.g., step (d)(1) of claim 20); that the amplifying step occurs in less than 4 hours (e.g., step (d)(2) of claim 20); or that the host cells divide less than 6 times (e.g., step (d)(3) of claim 20).

The Office cites Srivastava, the secondary reference, only for disclosing "... varying the stringency of the elution medium in recovering phage (at page 5 of the Office Action)." Srivastava, therefore, fails to rectify the deficiencies of Sawyer. Since Sawyer and Srivastava, individually or in combination, fail to teach or suggest the claimed methods, the references do not render claims 1-7, 9-15 and 20-28 obvious.

Rejection of claims 1-7, 9-15, 18, 20-24 and 26-28. At page 6 of the Office Action, the Office rejects claims 1-7, 9-15, 18, 20-24 and 26-28 as allegedly being obvious over Sawyer in view of U.S. Pat. No. 6,423,538 B1 ("Wittrup"). Applicants disagree and respectfully traverse this rejection.

The deficiencies of Sawyer are discussed above. As the Office merely cites Wittrup for teaching "... the use of mutator strains with phage as a means of producing randomized

displayed peptides (at page 6 of the Office Action)," Wittrup fails to remedy the deficiencies of Sawyer. Thus, Sawyer and Wittrup, individually or combined, fail to teach or suggest the claimed methods.

For at least the reasons stated above, Applicants submit that the Office has failed to establish a *prima facie* case of obviousness against the claims based on Sawyer in view of Srivastava (claims 1-7, 9-15 and 20-28) or Wittrup (claims 1-7, 9-15, 18, 20-24 and 26-28), and withdrawal of these rejections is respectfully requested.

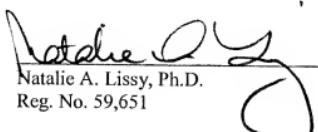
CONCLUSION

Applicants respectfully submit that all examined claims are in condition for allowance, which action is expeditiously requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do Applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

The fee in the total amount of \$1170 for excess claim fees is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please any other charges or credits to deposit account 06-1050, referencing Attorney's Docket No. 10280-053001.

Respectfully submitted,

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